

New §371 Application
Based on PCT/EP00/08129
Filed February 20, 2002
Markl, et al.

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SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),

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SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h"),
SEQ ID NO:157 (complete HtH2 domain a);

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).

50. Pharmaceutical composition comprising a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, and comprising at least one intron sequence, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),

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SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),

SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h"),
SEQ ID NO:157 (complete HtH2 domain a);

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the

- immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
 - (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
 - (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
 - (g) combinations of several of the DNA sequences described under (a) to (f).

Please amend Claims 3 through 6, 10, 12, 13, 15 through 17, 20, 23, 24, 26, 37, 38, 43, 44, 46, and 47 so that they read as follows.

3. (Amended) Nucleic acid molecule according to claim 1, characterized in that the hybridization described under (b), (d) or (ii) is carried out under stringent conditions.

4. (Amended) Nucleic acid molecule according to claim 1 , characterized in that the nucleic acid molecule described under (e) is at least 80% homologous to one of the nucleic acid sequences described under (a) .

5. (Amended) Nucleic acid molecule according to claim 1 , characterized in that the nucleic acid molecule described under (e) is at least 90 % homologous to one of the nucleic acid sequences described under (a) .

6. (Amended) Nucleic acid molecule according to claim 1 , characterized in that the nucleic acid molecule described under (e) is at least 95 % homologous to one of the nucleic acid sequences described under (a) .

10. (Amended) Nucleic acid molecule according to claim 1, characterized in that it is a deoxyribonucleic acid molecule.

12. (Amended) Construct according to claim 49, further comprising a promoter which is suitable for expression control, the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof being under the control of the promoter.

13. (Amended) Construct according to claim 49 further comprising a nucleic acid sequence which codes for an antigen and is coupled directly to the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof.

15. (Amended) Construct according to claim 49 , wherein the construct comprises at least a part of a vector, the vector being selected from: bacteriophages, adenoviruses, vaccinia viruses, baculoviruses, SV40 virus and retroviruses.
16. (Amended) Construct according to claim 49 , wherein the construct furthermore comprises a His tag-coding nucleic acid sequence and the expression of the construct leads to the formation of a fusion protein with a His tag.
17. (Amended) Host cell containing a construct according to claim 49, wherein the host cell is a prokaryotic or eukaryotic cell suitable for expression of the construct.
20. (Amended) Process for the preparation of a haemocyanin polypeptide, wherein the nucleic acid molecule according to claim 1 or a construct comprising said nucleic acid is expressed in a suitable host cell and the protein is isolated, if appropriate.
23. (Amended) Process according to claim 20, characterized in that the expression is carried out in a host cell containing a construct comprising said nucleic acid molecule .
24. (Amended) Haemocyanin polypeptide, comprising an amino acid sequence which is coded by one or more of the nucleic acid molecules according to claim 1.
26. (Amended) Recombinant haemocyanin polypeptide, obtainable by the process according to claim 20 or modifications thereof.

37. (Amended) Pharmaceutical composition according to claim 50, characterized in that it is used for gene therapy treatment of tumours.

38. (Amended) Pharmaceutical composition, comprising a haemocyanin polypeptide according to claim 24 and physiologically tolerated additives.

43. (Amended) Use of a haemocyanin polypeptide according to claim 24 as a carrier substance for medicaments.

44. (Amended) Liposome, comprising a nucleic acid molecule according to claim 1, a construct comprising said nucleic acid molecule or a haemocyanin polypeptide comprising an amino acid sequence which is coded by one or more of said nucleic acid molecules.

46. (Amended) Antibodies, obtainable by immunization of a test animal with the recombinant haemocyanin polypeptide according to claim 24.

47. (Amended) Screening method for identification of tumour-specific DNA in a cell, comprising:

- a) bringing cell DNA and/or cell protein into contact with a probe comprising the nucleic acid sequence according to claim 1 and/or the antibody obtainable by immunization of a test animal with the recombinant haemoganic polypeptide comprising an amino

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acid sequence which is coded by one or more of said nucleic acid molecule and

b) detecting the specific binding.

REMARKS

Prosecution and consideration of the claimed subject matter in the accompanying patent application is respectfully requested.

I. The Amendments

The attached English translation of the abstract and claims as filed in the corresponding international patent application were amended to conform to standard U.S. practice. As a result, the originally-filed English translation of Claims 3 through 6, 10, 12, 13, 15 through 17, 20, 23, 24, 26, 37, 38, 43, 44, 46, and 47 were amended, Claims 11 and 36 were cancelled and new Claims 49 and 50 were introduced in place of the cancelled claims.

A copy of the claims showing the amendments effected by this substitution of the claims is enclosed. The substitute claims derive their support from the claims as originally filed with amendments as to form rather than substance.

Claims 1-10, 12-35, and 37-50 are in the case and are before the Examiner. It is thus seen that no new matter has been presented. A complete, clean copy of the claims before the Examiner is enclosed herewith.